

THERMODYNAMIC AND KINETIC EVALUATIONS OF RADICAL STABILITIES

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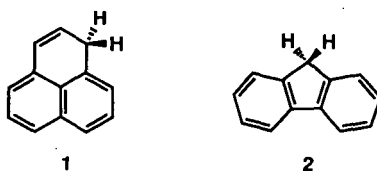
Abstract When inserted into appropriate thermochemical cycles, redox data have proven invaluable in the studies of heterolytic and homolytic bond strengths. Judicious use of microelectrode-based cyclic voltammetry also enables determinations of the rates of degradation for several classes of solution phase reactive intermediates. Described in this paper are (a) new bond strength results from our group that shed light on the effects of β -substituents on the thermodynamic stabilities of various carbon- and nitrogen- centered radicals; and (b) recent evaluations of second-order rate constants for dimerization reactions of electrochemically-generated carbon-centered radicals.

Introduction

It has been shown that insertion of selected acid-base¹ and redox data into thermochemical cycles² (as in eq 1³) results in accurate (± 1.2 kcal/mol) determinations of relative and absolute

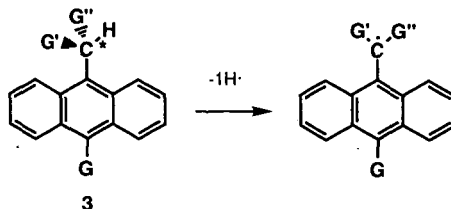
$$\Delta G^{\circ}_{\text{hom}}(\text{R-H}) = 1.36pK_a(\text{R-H}) + 23.1[E_{\text{NHE}}(\text{R}^{\bullet}/\text{R}^{\circ})] + 57.2 \text{ kcal/mol} \quad (1)$$

free energies of homolysis³ [$\Delta G^{\circ}_{\text{hom}}(\text{R-H})$] for several classes of reactions.⁴ For example, we have shown that the C-H homolytic bond dissociation energies for phenalene (1) and its isomeric



analogue fluorene (2) are 65 and 80 kcal/mol, respectively.⁵ These data are of interest due to the persistence of the planar phenalenyl radical, as well as the continuing interest in polycyclic aromatic chemistry.

In other published work, evidence for the importance of charge separation as it pertains to radical stabilization was provided from studies of the effects of electron-withdrawing and electron-donating moieties on #9C-H anthrylmethyl homolytic bond strengths, for the substituted anthracenes (3) depicted below. Specifically, while the singular presence of $G=\text{CN}$, or $G=\text{PhO}$,

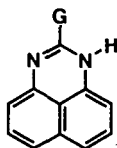


weakens the indicated (*) bond by ca. 1.5 and 3 kcal/mol, respectively, the simultaneous presence of these substituents weakens the same bond by ca. 9 kcal/mol.⁶ These results provided support for the idea that appropriately substituted solution-phase radicals can be stabilized via delocalization of the unpaired electron even when that delocalization results in some charge separation.⁶

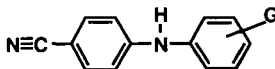
Results and Discussion

N-H Bond Strengths

In light of the importance of nitrogen in the chemistry of coal, we have therefore endeavored to collect the pK_a (R-H) and $E_{NHE}(R^{\cdot}/R^+)$ data that enable determination of the $\Delta G^{\cdot}_{hom}(R-H)$ values for several variously substituted perimidines (4), a nitrogen analogue of



4



5

phenalene, as well as several diphenylamine analogues (5). The bond strengths for 4 shed important light on the effects of β -substituents on N-H bond strengths, while the analogous data for 5 provide new insights into the effects of aryl substituents on N-H bond strengths. The acidity and bond strength data are listed in Tables I and II.

β -Effects on N-H Bond Strengths Inspection of the acidity data in Table I reveals that β -substituents have relatively large effects on N-H equilibrium acidities. For example, 2-methylperimidine ($pK_a=17.2$) is ca. 8 kcal/mol less acidic than 2-chloroperimidine ($pK_a=11.4$). The magnitude of the acidifying effects of the β -substituents is surprising since there we are not aware of the existence of resonance contributing structures in which formal negative charge is present on the sp^2 -hybridized #2-carbon atom. It is also of interest to compare the C-H pK_a for phenalene (18.25) with the N-H pK_a for perimidine (16.2). The 2 pK unit greater acidity of the nitrogen analogue is not surprising in light of the pK_a 's for fluorene (22.6) and carbazole (19.9),¹ and is readily explained by the greater electronegativity of nitrogen, compared to carbon.

Examination of the $\Delta G^{\cdot}_{hom}(R-H)$ data for the substituted perimidines reveals that the substituent effects on homolytic bond strengths are substantially smaller (by a factor of three) than the substituent-induced variation in the pK_a 's for the same species. These results are consistent with a hypotheses which states that inductive (de)stabilizing effects of substituents on radical stabilities are small, compared to the resonance effects of those same substituents. The $\Delta G^{\cdot}_{hom}(R-H)$ value for carbazole (88 kcal/mol),⁷ when compared to the $\Delta G^{\cdot}_{hom}(R-H)$ value for perimidine (75 kcal/mol), is reasonable in light of the $\Delta G^{\cdot}_{hom}(R-H)$ values for fluorene and phenalene (76 and 61 kcal/mol, respectively). Both sets of data are consistent with the notion that N-H bonds are generally stronger, in a homolytic sense, than C-H bonds found in structurally similar species.

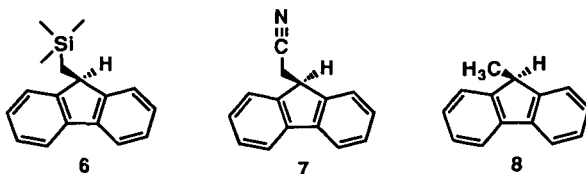
Remote Substituent Effects on N-H Bond Strengths Inspection of the pK_a and $\Delta G^{\cdot}_{hom}(R-H)$ data in Table II reveals that substituents that weaken N-H bonds in 5 in an acid-base sense (i.e. electron-withdrawing substituents such as 4-nitro, 4-cyano, and 3-chloro) strengthen the same N-H bonds in a free radical (i.e. homolytic) sense. Although the pK_a results are readily understood and indicative of planarity in the diphenylamine nitranion (Hammett treatment of the data yields a linear plot with a ρ value of 2.6, $r=0.99$),⁸ the $\Delta G^{\cdot}_{hom}(R-H)$ values are perhaps best rationalized by noting the electron-deficient nature of the nitrogen-centered radicals.

In an effort to comprehend the $\Delta G^{\cdot}_{hom}(R-H)$ values for 5, it is instructive to compare the $\Delta G^{\cdot}_{hom}(R-H)$ data in Table II with $\Delta G^{\cdot}_{hom}(R-H)$ data for (4-nitrophenyl)phenylamine; (4-cyanophenyl)phenylamine; (3-chlorophenyl)phenylamine; diphenylamine; (4-methylphenyl)phenylamine; and (4-methoxyphenyl)phenylamine (87,⁷ 85, 84,⁷ 83,⁷ 83,⁷ and 82⁷ kcal/mol, respectively). Here too the acidifying electron-withdrawing substituents appear to strengthen the diphenylamine N-H bond in a homolytic sense. The results therefore suggest that nitranion-stabilizing substituents act to destabilize nitrogen-centered radicals. For both sets of $\Delta G^{\cdot}_{hom}(R-H)$ data, a complex interplay of resonance and inductive effects must be considered. Therefore, we are currently investigating the N-H bond strengths for several additional diphenylamines, including ten different nitrodiphenylamines, in an attempt to gain additional understanding of these phenomena.

C-H Bond Strengths

The previous section described results which indicate that more data are needed regarding resonance and inductive effects as they pertain to homolytic bond strengths and radical stabilities. In an effort to separate resonance and inductive effects, we have synthesized and evaluated the

bond cleavage chemistry for 9-(trimethylsilylmethyl)fluorene (**6**) and 9-(cyanomethyl)fluorene (**7**).



The relevant pK_a and $\Delta G^*_{\text{hom}}(\text{R-H})$ data for **6** and **7**, along with similar data for 9-methylfluorene (**8**), are listed in Table III.

Inspection of the data in Table III reveals that the β -trimethylsilyl and β -cyano substituents both acidify 9-methylfluorene. These results are consistent with the notion of an enhanced electron accepting ability for silicon atoms⁹ and cyano moieties (relative to hydrogen). On the other hand, comparison of the $\Delta G^*_{\text{hom}}(\text{R-H})$ data for **6**, **7**, and **8** reveals that the electron-withdrawing β -cyano substituent strengthens the #9C-H bond in fluorene by ca. 2 kcal/mol, while the β -trimethylsilyl substituent appears to weaken the same bond by about 3 kcal/mol. In other work, we have shown that the β -trimethylsilylmethyl and β -cyano substituents have somewhat similar effects on fluorenyl cation stabilities.^{10a} Specifically, β -trimethylsilylmethyl weakens the #9C-H bond, in a heterolytic cation-hydride forming sense, by 8 kcal/mol (relative to hydrogen), while β -cyano strengthens the same bond by 3 kcal/mol.^{10a} It appears, then, that the inductive and/or hyperconjugative effects of these two β -substituents on radical stabilities is similar to their effects on carbocation stabilities, in suggesting that (1) electron-withdrawing inductive effects destabilize carbon-centered radicals; and (2) electron-donating hyperconjugative effects stabilize carbon-centered radicals. These results provide additional evidence for rationalizing much of the chemistry of carbon-centered radicals as if they were electron-deficient species. We are currently examining several other β -substituted organic molecules in an effort to better understand these results.

Kinetics of Radical Dimerizations

A limitation of bond strength data obtained from thermochemical cycles that utilize irreversible redox potentials is that the peak potentials are not truly thermodynamic. This fact introduces some degree of uncertainty in bond strengths obtained using irreversible data. That the irreversible peak potentials (obtained at scan rates of 0.1 V/s) for various nitranion oxidations were nearly equal to the reversible $E_{1/2}$ values (obtained at scan rates of 1,000 V/s) for the same oxidations provided some evidence for the viability of irreversible potentials when used judiciously.^{10b} In addition, data obtained using the FSCV technique can be used to derive rate constants for the chemical reactions that follow the initial electrochemical reaction.

For example, shown in Fig 1 are two CV traces for the oxidation of the 9-(2-methylphenyl)fluorenyl anion. Examination of Fig 1 reveals that the carbanion oxidation is fully reversible at 1,000 V/s scan rates, but essentially irreversible at 0.1 V/s scan rates. Use of the equations developed by Nicholson and Shain¹¹ enables evaluation of the velocity of the reaction that removes the electrochemically generated radical from solution (*via* a second-order reaction) prior to its reduction on the reverse scan. With a microelectrode-equipped apparatus, second-order rates as high as $10^8 \text{ M}^{-1}\text{s}^{-1}$ are accessible. Listed in Table IV are rates determined in this way for the second order reactions of variously substituted fluorenyl radicals that have been generated anodically at a platinum working electrode.

Steric Effects on Radical Dimerizations Examination of the rate data listed in Table IV reveals that the tertiary 9-methylfluorenyl radical dimerizes¹² at the same rate as the 9-cyanofluorenyl and 9-phenylfluorenyl radicals, since the uncertainty in the rates listed in Table IV is estimated to be ca. $\pm 10\%$. Significantly, none of these species dimerizes at the diffusion-limited rate in DMSO (estimated at $2 \times 10^9 \text{ M}^{-1}\text{s}^{-1}$). It is likely that solvation effects and solvent reorganization plays some role in the slight rate retardation.

Comparison of the k_2 values for 9-*tert*-butylfluorenyl and 9-methylfluorenyl radicals (5×10^5 and 3×10^7 , respectively) provides direct evidence for the importance of steric effects on radical persistence. Evidently, the sterically demanding 9-*tert*-butyl group slows the dimerization rate by about two powers of ten (compared to 9-methyl), despite the fact that the homolytic bond strength data for these two species indicates that the 9-*tert*-butylfluorenyl radical is about 4 kcal/mol *less stable* than the 9-methylfluorenyl radical.

Furthermore, molecular models as well as bond strength data for 9-phenylfluorene, 9-(2-

methylphenyl)fluorene, and 9-mesitylfluorene [$\Delta G^{\circ}_{\text{hom}}(\text{R-H})=70, 71, \text{ and } 72 \text{ kcal/mol}$, respectively] suggest that the presence of *ortho* methyl groups on the #9-phenyl moiety causes the phenyl ring in 9-phenylfluorenyl radicals to twist out of the plane of the fluorene. Kinetic evidence for this assertion is provided in Table IV, since the k_2 values for 9-phenylfluorenyl, 9-(2-methylphenyl)fluorenyl, and 9-mesitylfluorenyl radicals are 1×10^7 , 8×10^3 , and $1 \text{ M}^{-1}\text{s}^{-1}$, respectively). These results (i.e. solution-phase dimerization rates for delocalized fluorenyl radicals) are the first of their kind, and provide additional evidence for the notion that radical persistence is largely a kinetic phenomenon that is usually associated with steric hindrance in the immediate vicinity of the unpaired electron. We are continuing studies of the kinetics of dimerization reactions of delocalized carbon-centered radicals, and have also embarked on similar evaluations of the dimerization reactions of delocalized nitrogen-centered radicals.

Experimental Section

DMSO was purified, potassium dimslyate was synthesized, and the $\text{p}K_a$ and redox experiments were carried out as described previously.^{5,6,10} $\Delta G^{\circ}_{\text{hom}}(\text{R-H})$ values calculated as described in Reference 10a. Substrates synthesized as described in references 6, 8, and 10. The PMV device was using specifications described by Griller et al.¹⁴ Reference 12 (submitted to *J. Org. Chem.*) contains experimental details of the FSCV device.

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Table I. Dimethyl Sulfoxide (DMSO) Acidity (pK_a and ΔpK_a) and Homolytic Bond Strength [$\Delta G^{\circ}_{\text{hom}}(\text{R-H})$ and $\Delta\Delta G^{\circ}_{\text{hom}}(\text{R-H})$] Values for 2-Substituted Perimidines (4).

Substrate	pK_a	ΔpK_a (kcal/mol)	$\Delta G^{\circ}_{\text{hom}}(\text{R-H})$ (kcal/mol)	$\Delta\Delta G^{\circ}_{\text{hom}}(\text{R-H})$ (kcal/mol)
2-methylperimidine	17.2	+1.4	75	0
perimidine	16.2	(0)	75	(0)
2-phenylperimidine	14.7	-2.0	73	-2
2-thiomethylperimidine	13.3	-4.0	72	-3
2-chloroperimidine	11.4	-6.6	73	-2

Table II. Dimethyl Sulfoxide (DMSO) Acidity (pK_a and ΔpK_a) and Homolytic Bond Strength [$\Delta G^{\circ}_{\text{hom}}(\text{R-H})$ and $\Delta\Delta G^{\circ}_{\text{hom}}(\text{R-H})$] Values for Remotely Substituted Diphenylamines (5).

Substrate	pK_a	ΔpK_a (kcal/mol)	$\Delta G^{\circ}_{\text{hom}}(\text{R-H})$ (kcal/mol)	$\Delta\Delta G^{\circ}_{\text{hom}}(\text{R-H})$ (kcal/mol)
4-methoxyphenyl-4-cyanophenylamine	21.2	+1.1	84	-1
4-methylphenyl-4-cyanophenylamine	20.8	+0.5	85	0
phenyl-4-cyanophenylamine	20.4	(0)	85	(0)
3-chlorophenyl-4-cyanophenylamine	18.9	-2.1	87	+2
bis(4-cyanophenyl)amine	17.4	-4.1	88	+3
4-nitrophenyl-4-cyanophenylamine	15.5	-6.7	89	+4

Table III. Dimethyl Sulfoxide (DMSO) Acidity (pK_a and ΔpK_a) and Homolytic Bond Strength [$\Delta G^{\circ}_{\text{hom}}(\text{R-H})$ and $\Delta\Delta G^{\circ}_{\text{hom}}(\text{R-H})$] Values for Variously Substituted Fluorenes 6, 7, and 8.

Substrate	pK_a	ΔpK_a (kcal/mol)	$\Delta G^{\circ}_{\text{hom}}(\text{R-H})$ (kcal/mol)	$\Delta\Delta G^{\circ}_{\text{hom}}(\text{R-H})$ (kcal/mol)
9-(trimethylsilylmethyl)fluorene	21.4	-1.6	69	-3
9-(cyanomethyl)fluorene	19.9	-3.7	74	+2
9-methylfluorene	22.6	(0)	72	(0)

Table IV. Dimethyl Sulfoxide (DMSO) Acidity (pK_a and ΔpK_a) and Homolytic Bond Strength [$\Delta G^{\circ}_{\text{hom}}(\text{R-H})$ and $\Delta\Delta G^{\circ}_{\text{hom}}(\text{R-H})$] Values for Variously Substituted Fluorenes 6, 7, and 8.

Radical ($\text{R}\cdot$)	$\Delta G^{\circ}_{\text{hom}}(\text{R-H})$ (kcal/mol)	$\Delta\Delta G^{\circ}_{\text{hom}}(\text{R-H})$ (kcal/mol)	k_2 ($\text{M}^{-1}\text{s}^{-1}$)
9-methylfluorenyl	72	(0)	3×10^7
9-cyanofluorenyl	71	-1	2×10^7
9-phenylfluorenyl	70	-2	1×10^7
9- <i>tert</i> -butylfluorenyl	76	+4	5×10^5
9-(2-methylphenyl)fluorenyl	71	-1	8×10^3
9-mesitylfluorenyl	72	0	<1

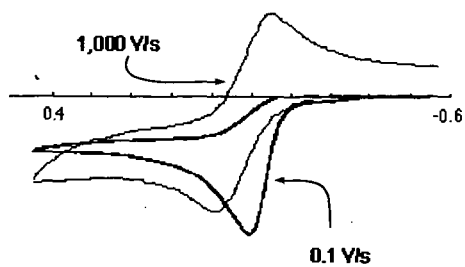


Fig 1. CV traces (at 1000 and 0.1 V/s scan rates) for the anodic oxidation of the 9-(2-methylphenyl)fluorenone anion.